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EXAMINER	
NEGIN, RUSSELL SCOTT	
ART UNIT	PAPER NUMBER
1631	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/660,110	OLDHAM ET AL.	
	Examiner	Art Unit	
	RUSSELL S. NEGIN	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 April 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *20,23-34 and 36-55* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20, 23-34, and 36-55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Comments

Applicants' request for reconsideration in the communication filed on 1 April 2008 is acknowledged and the amendments are entered.

Claims 20, 23-34, and 36-55 are pending and examined in the instant Office action.

Withdrawn Rejections

The rejections of claims 20, 23-32 and 47-55 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention are withdrawn in view of amendments filed on 1 April 2008.

The rejections of claims 20, 23, and 45-46 under 35 U.S.C. 102(b) as being anticipated by Kobayashi et al. [Journal of Chromatography, volume 480, 1989, pages 179-184] are withdrawn in view of amendments filed on 1 April 2008.

The rejections of claims 24, 33-34, 36, and 47 under 35 U.S.C. 103(a) as being unpatentable over Kobayashi et al. as applied above, and further in view of Tomlinson et al. [Electrophoresis, 1994, volume 15, pages 62-71] are withdrawn in view of amendments filed on 1 April 2008.

The rejections of claims 28-29, 31-32, 40-41, 43-44, 51-52, and 54-55 under 35 U.S.C. 103(a) as being unpatentable over Kobayashi et al. in view of Tomlinson et al. as

applied above, and further in view of Photomultiplier Tubes [Hamamatsu Brochure, pages 1-15, July 2002] are withdrawn in view of amendments filed on 1 April 2008.

The rejections of claims 30, 42, and 53 under 35 U.S.C. 103(a) as being unpatentable over Kobayashi et al. in view of Tomlinson et al. in view of Photomultiplier tubes as applied above, in further view of Priebe [19th Annual Symposium of Frequency Control, 1965, pages 487-508] are withdrawn in view of amendments filed on 1 April 2008.

The rejections of claims 25-26, 37-38, and 48-49 under 35 U.S.C. 103(a) as being unpatentable over Kobayashi et al. in view of Tomlinson et al. as applied above, and further in view of Tacklind et al [US PGPUB 2003/0101605; issued 5 June 2003; filed 4 December 2001] are withdrawn in view of amendments filed on 1 April 2008.

The rejections of claims 27, 39, and 50 under 35 U.S.C. 103(a) as being unpatentable over Kobayashi et al. in view of Tomlinson et al. in view of Tacklind et al. as applied to above, and further in view of Pierre et al. [IEEE Acoustics, Speech, and Signal Processing. 1995, pages 1900-1903] are withdrawn in view of amendments filed on 1 April 2008.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

35 U.S.C. 103 Rejection #1:

Claims 20, 23-24, 33-34, 36 and 45-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Savory et al. [Clinical Chemistry, volume 14, 1968, pages 132-144] in view of Chen et al. [Genome Research, 1998, volume 8, pages 549-556].

The method of claims 20 and 45 are drawn to improving the assessment of a plurality of types of specific particles in a sample using a photodetector. This photodetector detects particles, each type of particle being labeled with a specific probe. A scaling procedure with two configurations of the photodetector is used such that scaling may be used between configurations to estimate the signals out of the dynamic range of the photodetector in a specific configuration.

Claims 23-24 and 46-47 are further limiting with regards to scaling and combining the signals between the two types of configurations.

The method of claim 33 is drawn to extending the range of a photodetector for the assessment of a plurality of types of specific particles. This photodetector detects particles. A scaling procedure with two configurations of the photodetector is used such that scaling may be used between configurations to estimate the signals out of the dynamic range of the photodetector in a specific configuration.

Claim 34 is further limiting wherein the first component of the detectable signal is stronger than the second component.

Claim 36 is further limiting wherein scaling the first output signal allows representation of both the first and second components when the dynamic range associated with the detector is limiting and would not be able to measure the first component at the first configuration

The study of Savory et al. investigates an improved procedure for the determination of serum ethanol by gas chromatography. Specifically, Figure 5 on page 141 of Savory et al. illustrates the chromatograms of a single sample of six different compounds obtained in two different configurations of the GC apparatus (Helium flow= 75 ml per min and 45 ml per min, respectively). In this second configuration, the peaks are lower in height than in the first configuration (i.e. while the y axis or dynamic ranges of the chromatograms go to 8 cm and 10 cm, respectively for each of the two configurations, some of the peaks in the first configuration would be out of the dynamic range of the detector in the second configuration).

However, Savory et al. does not show actual scaling between the configurations, nor does he use a photodetector to detect the presence of particles labeled with probes (Savory et al. use a detector)

The study of Chen et al. is a homogeneous ligase mediated DNA diagnostic test.

Figures 1 and 2 of Chen et al. illustrate an assay and the result of a DOL assay with FRET detection using probes to label the nucleic acid segments. Figure 3 of Chen et al. illustrates the fluorescence intensity profiles of a PCR-DOL assay.

It would have been obvious for someone of ordinary skill in the art at the time of the instant invention to modify the gas chromatography study of Savory et al. by scaling peak size to obtain signals out of range of the detector because areas under each peak in a gas chromatogram (i.e Figure 5 of Savory et al.) are directly proportional to the amount of sample injected, and therefore by taking the ratio of area of peak A to the area of peak B in the second configuration (where both peaks are within the dynamic range of the detector) would have been useful in deducing the height of peak A in the first configuration wherein the area of peak B in the first configuration is known. It would have been further obvious for someone of ordinary skill in the art at the time of the instant invention to modify the detector analysis of Savory et al. by use of the photodetector analysis of Chen et al. because it is obvious to substitute known elements in the prior art to yield a predictable result. In this instance, both types of detector yield the predictable result of sample quantities. There would have been a reasonable expectation of success in combining Savory et al. and Chen et al. because in this instance, the detector and photodetector are used for the same purpose.

Response to Arguments:

Applicant's arguments with respect to the instant claims have been considered but are moot in view of the new ground(s) of rejection.

35 U.S.C. 103 Rejection #2:

Claims 28-29, 40-41, and 51-52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Savory et al. in view of Chen et al. as applied to claims 20, 23, 24, 33, 34, 36, and 45-47 above, and further in view of Tomlinson et al [Electrophoresis, 1994, volume 15, pages 62-71].

Claims 28, 40, and 51 are further limiting wherein the detector is a charge multiplier and the first configuration comprises an operating voltage V1.

Claims 29, 41, and 52 are further limiting wherein the second configuration comprised an operating voltage V2, wherein the operating voltage V2 is higher (or lower for claim 52) than the operating voltage V1.

The studies of Savory et al. and Chen et al. make obvious the measurement of signals of particle using photodetectors/detectors, as discussed above.

Tomlinson et al. discloses two separate voltages for the two separate configurations disclosed in Figures 3 and 4; one configuration uses a voltage of 20kV, the second uses a voltage of 30 kV- a voltage greater than in the first configuration. (For claim 52, the configurations are interpreted to be reversed).

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the chromatography study of Savory and the photodetector study of Chen et al. by use of the electropherograms analyzed at differing voltages using a photodetector of Tomlinson et al. wherein the motivation would have been that altering voltages in measuring the composition of a sample is an additional means of assessing and comparing relative concentrations of each species of particle in a sample; for example, changing the voltage in Figures 3 and 4 of Tomlinson et al. improves the resolution of the electropherogram.

Response to arguments:

Applicant's arguments filed 1 April 2008 have been fully considered but they are not persuasive. While applicant addresses the alleged deficiencies of this rejection in terms of the Tomlinson et al. reference, the newly applied references of Savory et al. and Chen et al. address these alleged deficiencies.

35 U.S.C. 103 Rejection #3:

Claims 31-32, 43-44, and 54-55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Savory et al. in view of Chen et al. in view of Tomlinson et al. as applied to claims 20, 23, 24, 28-29, 33, 34, 36, 40-41, 45-47, and 51-52 above, and further in view of Photomultiplier Tubes [Hamamatsu Brochure, pages 1-15, July 2002].

Claims 31, 43, and 54 are further limiting wherein the charge multiplier comprises photomultiplier tubes.

Claims 32, 44, and 55 are further limiting wherein the charge multiplier comprises a charge intensifier.

The studies of Savory et al., Chen et al., and Tomlinson et al. make obvious the measurement of signals of particle using photodetectors, as discussed above.

However, Savory et al., Chen et al., and Tomlinson et al. do not disclose charge multipliers, specifically, in the forms of photomultiplier tubes and charge intensifiers.

The catalog "Photomultiplier tubes" discusses uses and sales of photomultiplier tubes and charge intensifiers throughout the brochure.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the photodetector studies of Savory et al., Chen et al., and Tomlinson et al. by use of the photomultiplier tubes and charge intensifiers of the Hamamatsu Brochure because it would have been obvious to apply a known technique to a known method to yield a predictable result. In this instance, it would have been obvious to apply the techniques of using photomultipliers and charge intensifiers to the methods of signal analysis of Savory et al., Chen et al., and Tomlinson et al. to result in modified electropherogram absorbance intensities. There would have been a reasonable expectation of success in incorporating the photomultiplier tubes into the detectors of Savory et al., Chen et al., and Tomlinson et al. because such photomultiplier tubes and charge multipliers provide an alternative means for measuring the intensities of particles in a mixture (i.e. a photomultiplier detects photons and converts them into electropherograms or electrical signals).

Response to Arguments:

Applicant's arguments with respect to the instant claims have been considered but are moot in view of the new ground(s) of rejection.

35 U.S.C. 103 Rejection #4:

Claims 30, 42, and 53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Savory et al. in view of Chen et al. in view of Tomlinson et al. in view of Photomultiplier tubes as applied to claims 20, 23-24, 28-29, 31-34, 36, 40-41, 43-47, 51-52, and 54-55 above, in further view of Priebe [19th Annual Symposium of Frequency Control, 1965, pages 487-508].

Claims 30, 42, and 53 are further limiting wherein the combining to determine comprises determining a scaled value N1 of the first output signal based on the third output signal and the relationship log (N1) = m log (V2/V1) wherein m represents a slope of a curve obtained by plotting the multiplier's gain versus the voltage in a log-log manner.

The studies of Savory et al., Chen et al., Tomlinson et al. and the Photomultiplier Tube brochure make obvious the measurement of signals of particle using photomultipler tubes, as discussed above.

Savory et al., Chen et al., Tomlinson et al. and the Photomultiplier Tube brochure do not discuss the specific relation in the instant set of claims.

The study of Priebe investigates the attenuation and resistance measurements of unwanted modes of quartz crystals.

Specifically, equation 2 of Priebe shows that the attenuation of the signal from the crystal (in Decibel) is proportional to the logarithm of the ratios of two voltages with the proportionality constant (m) being 20.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the photodetector measurements using photomultiplier tubes of Savory et al., Chen et al., Tomlinson et al. and Hamamatsu (i.e. Brochure) by further use of the relation of Priebe because it would have been obvious to apply a known technique to a known method to yield a predictable result. In this instance, it would have been obvious to apply the known signal attenuation techniques of Priebe to the photodetector system of Savory et al., Chen et al., Tomlinson et al. to yield the predictable outcome of comparably attenuated signals. There would have a reasonable expectation of success in combining the relations of Priebe with photomultiplers tubes and detectors of Savory et al., Chen et al., Tomlinson et al. because the relation of Priebe allows for the attenuation of a multiplier's gain.

Response to Arguments:

Applicant's arguments with respect to the instant claims have been considered but are moot in view of the new ground(s) of rejection.

35 U.S.C. 103 Rejection #5:

Claims 25-26, 37-38, and 48-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Savory et al. in view of Chen et al. in view of Tomlinson et al. as

applied to claims 20, 23, 24, 28-29, 33, 34, 36, 40-41, 45-47, and 51-52 above, and further in view of Tacklind et al [US PGPUB 2003/0101605; issued 5 June 2003; filed 4 December 2001].

Claims 25, 37, and 48 are further limiting wherein the detector is a charge-coupled device and the first configuration comprises an exposure duration T1.

Claims 26, 38, and 49 are further limiting wherein the second configuration comprises an exposure duration T2, wherein the exposure duration T2 is longer (or shorter for claim 49) than the exposure duration T1.

The studies of Savory et al., Chen et al., and Tomlinson et al. make obvious the measurement of signals of particle using photodetectors, as discussed above.

Tomlinson et al. plots two separate migration times for the two separate configurations, with one set (i.e. CE-DAD or Figure 4) having a greater length in migration time (T2) than solely CE (CE is Figure 3, or T1). Depending on which of claims 48-49 are being analyzed, the configuration assignments could be reversed so that T2 is shorter in duration that T1.

However, Savory et al., Chen et al., and Tomlinson et al. do not disclose a charge multiplier.

The invention of Tacklind et al. studies servo-controlled automatic level and plumb tool and explains the use of charge coupled devices in paragraph [0060] where it is stated that "The position sensitive photo sensor can incorporate any of a number of commercially available position sensitive detectors sensitive to the detector light... Examples include charged coupled detectors (CCD)."

Consequently, charged coupled detectors are used to assist in analyzing signals from detectors.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the photodetector analyses of Savory et al., Chen et al. and Tomlinson et al. by use of the CCDs of Tacklind et al. because it is obvious to apply a known technique to a known method to yield a predictable result. In this instance, it would have been obvious to apply the known technique of using CCDs to analyze signals to the known method of using photodetectors to measure sample amount as in Savory et al., Chen et al. and Tomlinson et al. to yield the predictable result of modified spectra and a modified means of receiving the relevant signals. There would have been a reasonable expectation of success in combining a CCD of Tacklind et al. with the detectors and photodetectors of Savory et al., Chen et al. and Tomlinson et al. because the charge coupled device of Tacklind et al. allows an alternative means of measuring the intensities of particles and converting them into electrical signals.

Response to Arguments:

Applicant's arguments with respect to the instant claims have been considered but are moot in view of the new ground(s) of rejection.

35 U.S.C. 103 Rejection #6:

Claims 27, 39, and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Savory et al. in view of Chen et al. in view of Tomlinson et al. in view

of Tacklind et al. as applied to claims 20, 23-26, 28-29, 33, 34, 36-38, 40-41, 45-49, and 51-52 above, and further in view of Pierre et al. [IEEE Acoustics, Speech, and Signal Processing. 1995, pages 1900-1903].

Claims 27, 39 and 50 are further limiting wherein the scaling of the first output signal comprises multiplying the first output signal value by a ratio of T2/T1.

The studies of Savory et al., Chen et al., Tomlinson et al., and Tacklind et al. make obvious the measurement of signals of particle using photodetectors, as discussed above.

The studies of Savory et al., Chen et al., Tomlinson et al., and Tacklind et al. do not teach multiplying the signal by a ratio of T2/T1.

The article of Pierre et al. studies the consideration in the autocalibration of quadrature receivers in which Figure 2 on page 1902 of Pierre et al. illustrates a log-log plot of the variance of the signal to noise ratio as a function of the ratio of two times. The purpose of the simulation plotted in Figure 2 of Pierre is to illustrate the variance in signal to noise ratio as observation time increases.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the photodetector analysis of Savory et al., Chen et al., Tomlinson et al., and Tacklind et al. by use of the time ratio simulation of Pierre et al. where the motivation would have been that Pierre et al. gives information regarding signal accuracy (in terms of variance in signal to noise ratio) as a function of observance time [see page 1903 of Pierre et al.]

Response to Arguments:

Applicant's arguments with respect to the instant claims have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the central PTO Fax Center. The faxing of such pages must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61

(November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)). The Central PTO Fax Center Number is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Negin, Ph.D., whose telephone number is (571) 272-1083. The examiner can normally be reached on Monday-Friday from 7am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisor, Marjorie Moran, Supervisory Patent Examiner, can be reached at (571) 272-0720.

Information regarding the status of the application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information on the PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/RSN/
Russell S. Negin, Ph.D.
7 July 2008

/Marjorie Moran/
Supervisory Patent Examiner, Art Unit 1631